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chain nodes : 12 13 14 15 17 ring nodes : $1 - 2 \quad 3 \quad 4 \quad 5 \quad 6 \quad 7 \quad 8 \quad 9 \quad 10 \quad 16$ chain bonds : $1 - 12 \quad 2 - 13 \quad 3 - 14 \quad 7 - 15 \quad 8 - 16 \quad 10 - 17$ ring bonds : $1 - 2 \quad 1 - 6 \quad 2 - 3 \quad 3 - 4 \quad 4 - 5 \quad 4 - 7 \quad 5 - 6 \quad 5 - 10 \quad 7 - 8 \quad 8 - 9 \quad 9 - 10$ exact bonds : $1 - 12 \quad 2 - 13 \quad 3 - 14 \quad 7 - 15 \quad 7 - 8 \quad 8 - 9 \quad 9 - 10$ isolated pring bonds : $1 - 12 \quad 2 - 13 \quad 3 - 14 \quad 7 - 15 \quad 7 - 8 \quad 8 - 9 \quad 9 - 10$ isolated ring systems : containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:Atom

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124

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L2 2 SEA SSS SAM L1

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68 ANSWERS

L3 68 SEA SSS FUL L1

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L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:534201 CAPLUS

DOCUMENT NUMBER: 141:71530

TITLE: Preparation of [1,7]naphthyridines as PDE4 inhibitors

INVENTOR(S): Denholm, Alastair; Keller, Thomas Hugo; Mccarthy, Clive; Press, Neil John; Taylor, Roger John

PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

	PATENT NO.									APPLICATION NO.								
	WO 2004055013																	
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB	, BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
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BK 200301/330					A 20051108				BR 2003-17330						20031215			
UN 1726215					T 20060125				CN 2003-80106300 JP 2004-560419						20031215			
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ER SOURCE(S):				MARI	PAT	141:	71530											

OTHER SOURCE(S): MARPAT 141:71530

AB The title compds. [I; Rl = axyl having up to 10 carbon atoms; NR2R3 = heterocyclyl having up to 10 ring atoms and having 1-4 heteroatoms in the ring system; in free or salt form] which are useful for treating conditions mediated by of phosphodiesterase type 4 or the down-regulation or inhibition of TNF-a release, particularly obstructive or inflammatory airways diseases, were prepared E.g., a 3-step synthesis of

3-[6-(3-hydroxypyrrolidin-1-yl)-[1,7]naphthyridin-8-yl]benzonitrile, starting from 6-amino-8-bromo-1,7-naphthyridine and 3-cyanophenylboronic acid, which showed ICSO of 1 nM for inhibition of PDE4D, was given. Pharmaceutical compns. that contain compds. I and processes for preparing the compds. I are claimed.

T 713145-28-9P 713145-30-3P 713145-47-2P

713145-56-3P 713145-62-1P

RE: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of [1,7]naphthyridines as PDE4 inhibitors)

RN 713145-28-9 CAPLUS CN 4-Piperidinecarboxy

4-Piperidinecarboxylic acid, 1-[8-(3-fluorophenyl)-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

RN 713145-30-3 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[8-(5-fluoro-2-methoxyphenyl)-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

RN 713145-47-2 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[8-[3-(methylthio)phenyl]-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

HO₂C

RN 713145-56-3 CAPLUS

CN Acetic acid, 2-[[1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-4piperidinyl]oxy]- (CA INDEX NAME)

 ${\rm HO_2C-CH_2-O^{'}}$

RN 713145-62-1 CAPLUS

CN 4-Piperidineacetic acid, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

HO2C-CH2

IT 713145-07-4P 713145-08-5P 713145-09-6P 713145-10-9P 713145-11-0P 713145-12-1P 713145-11-0P 713145-11-0P 713145-11-0P 713145-15-4P 713145-16-5P 713145-17-6P 713145-16-4P 713145-19-8P 713145-20-1P 713145-21-2P 713145-25-6P 713145-23-4P 713145-22-8P 713145-25-6P 713145-25-4P 713145-25-8P 713145-25-6P 713145-25-8P 713145-25-8P 713145-35-8P 713145-33-6P 713145-35-8P 713145-33-6P 713145-35-8P 71

713145-64-3P 713145-65-4P 713145-66-5P

713145-67-6P 713145-68-7P 713145-69-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of [1,7]naphthyridines as PDE4 inhibitors)

RN 713145-07-4 CAPLUS

CN Benzonitrile, 3-[6-(3-hydroxy-1-pyrrolidinyl)-1,7-naphthyridin-8-yl]- (CA INDEX NAME)

713145-08-5 CAPLUS RN

CN 1-Piperazinepropanenitrile, 4-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-, hydrochloride (1:1) (CA INDEX NAME)

NC-CH2-CH2

HC1

RN 713145-09-6 CAPLUS

4-Piperidinecarboxylic acid, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-, CN lithium salt (1:1) (CA INDEX NAME)

● Li

RN 713145-10-9 CAPLUS CN Benzonitrile, 3-[6-(1-piperaziny1)-1,7-naphthyridin-8-y1]-, hydrochloride (1:1) (CA INDEX NAME)

● HCl

- RN 713145-11-0 CAPLUS CN 4-Piperidinecarboxamide, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]- (CA INDEX NAME)
- NC N N
- RN 713145-12-1 CAPLUS
- CN Benzonitrile, 3-[6-(4-hydroxy-1-piperidiny1)-1,7-naphthyridin-8-y1]- (CA INDEX NAME)

RN 713145-13-2 CAPLUS

CN Benzonitrile, 3-[6-[4-(hydroxymethyl)-1-piperidinyl]-1,7-naphthyridin-8-yl]- (CA INDEX NAME)

RN 713145-14-3 CAPLUS

CN Benzonitrile, 3-[6-[4-(2-hydroxyethyl)-1-piperidinyl]-1,7-naphthyridin-8yl]- (CA INDEX NAME)

HO- CH2- CH2

RN 713145-15-4 CAPLUS

CN Benzonitrile, 3-[6-[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]-1,7-naphthyridin-8-yl]- (CA INDEX NAME)

Absolute stereochemistry.

- RN 713145-16-5 CAPLUS
- CN Benzonitrile, 3-[6-[4-[(tetrahydro-2-furany1)carbony1]-1-piperaziny1]-1,7-naphthyridin-8-y1]- (CA INDEX NAME)

- RN 713145-17-6 CAPLUS
- CN 3-Piperidinecarboxamide, 1-[8-(3-cyanopheny1)-1,7-naphthyridin-6-y1]- (CA INDEX NAME)

- RN 713145-18-7 CAPLUS
- CN Benzonitrile, 3-[6-(4-morpholinyl)-1,7-naphthyridin-8-yl]- (CA INDEX NAME)

RN 713145-19-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

RN 713145-20-1 CAPLUS

CN L-Proline, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

Absolute stereochemistry.

RN 713145-21-2 CAPLUS

CN Benzonitrile, 3-[6-(4-methyl-1-piperazinyl)-1,7-naphthyridin-8-yl)- (CA INDEX NAME)

RN 713145-22-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-, lithium salt (1:1) (CA INDEX NAME)

HO2C-CH2

• Li

RN 713145-23-4 CAPLUS

CN 1-Piperazineacetic acid, 4-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

RN 713145-24-5 CAPLUS

CN Benzonitrile, 3-[6-[4-(methylsulfonyl)-1-piperazinyl]-1,7-naphthyridin-8-yl]- (CA INDEX NAME)

RN 713145-25-6 CAPLUS
CN Benzonitrile, 3-[6-(3,5-dimethyl-1-piperazinyl)-1,7-naphthyridin-8-yl]-,
hydrochloride (1:1) (CA INDEX NAME)

● HCl

RN 713145-26-7 CAPLUS CN Benzonitrile, 3-[6-(4-ethyl-1-piperazinyl)-1,7-naphthyridin-8-yl]- (CA INDEX NAME)

RN 713145-27-8 CAPLUS

CN 3-Azetidinecarboxylic acid, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-(CA INDEX NAME)

HO₂C

RN 713145-29-0 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[8-(3-fluorophenyl)-1,7-naphthyridin-6-yl], sodium salt (1:1) (CA INDEX NAME)

....

Na

- RN 713145-31-4 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(5-fluoro-2-methoxypheny1)-1,7-naphthyridin-6-yl]-, potassium salt (1:1) (CA INDEX NAME)

HO₂C

K

- RN 713145-32-5 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3-chlorophenyl)-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

- RN 713145-33-6 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(5-chloro-2-methoxyphenyl)-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

- RN 713145-34-7 CAPLUS
- CN Benzoic acid, 3-[6-(4-morpholinyl)-1,7-naphthyridin-8-yl]- (CA INDEX NAME)

- RN 713145-35-8 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3-chlorophenyl)-1,7-naphthyridin-6-yl], sodium salt (1:1) (CA INDEX NAME)

● Na

- RN 713145-36-9 CAPLUS
- CN 3-Piperidinecarboxylic acid, 1-[8-(3-chlorophenyl)-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

- RN 713145-37-0 CAPLUS
- CN 3-Piperidinecarboxylic acid, 1-[8-(5-chloro-2-methoxyphenyl)-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

- RN 713145-38-1 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(5-chloro-2-methoxyphenyl)-1,7-naphthyridin-6-yl]-, sodium salt (1:1) (CA INDEX NAME)

● Na

RN 713145-39-2 CAPLUS

MeO.

CN 4-Piperidinecarboxylic acid, 1-[8-(3-methoxyphenyl)-1,7-naphthyridin-6-yl]-(CA INDEX NAME)

HO₂C

- RN 713145-40-5 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3,5-difluorophenyl)-1,7-naphthyridin-6yl]- (CA INDEX NAME)

HO₂C

- RN 713145-41-6 CAPLUS

HO₂C

RN 713145-42-7 CAPLUS

CN Acetic acid, 2-[[1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-4piperidinyl]oxy]-, potassium salt (1:1) (CA INDEX NAME)

HO2C-CH2-0

• K

RN 713145-43-8 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[8-(1,3-benzodioxol-5-yl)-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

HO₂C

RN 713145-44-9 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[8-[3-(trifluoromethoxy)phenyl]-1,7naphthyridin-6-yl]- (CA INDEX NAME)

HO₂C

- RN 713145-45-0 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3-chloro-4-fluorophenyl)-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

HO₂C

- RN 713145-46-1 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-4-methyl-, potassium salt (1:1) (CA INDEX NAME)

• K

- RN 713145-48-3 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-[3-(methylsulfinyl)phenyl]-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

- RN 713145-49-4 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-(8-phenyl-1,7-naphthyridin-6-yl)- (CA INDEX NAME)

- RN 713145-50-7 CAPLUS
- CN 4-Piperidineacetic acid, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-, potassium salt (1:1) (CA INDEX NAME)

K

- RN 713145-63-2 CAPLUS
- CN 1-Piperazine propanenitrile, 4-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

NC-CH2-CH2

- RN 713145-64-3 CAPLUS
- CN Benzonitrile, 3-[6-(1-piperazinyl)-1,7-naphthyridin-8-yl]- (CA INDEX NAME)

- RN 713145-65-4 CAPLUS
- CN 1-Piperazineacetic acid, 4-[8-(3-cyanopheny1)-1,7-naphthyridin-6-y1]- (CA INDEX NAME)

HO2C-CH2

- RN 713145-66-5 CAPLUS
- CN Benzonitrile, 3-[6-(3,5-dimethyl-1-piperazinyl)-1,7-naphthyridin-8-yl]-(CA INDEX NAME)

- RN 713145-67-6 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3-chlorophenyl)-1,7-naphthyridin-6-yl]-(CA INDEX NAME)

- HO₂C
- RN 713145-68-7 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(5-chloro-2-methoxyphenyl)-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

- HO₂C
- RN 713145-69-8 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-4-methyl- (CA INDEX NAME)

- IT 713145-51-8P 713145-52-9P 713145-55-2P 713145-57-4P 713145-58-5P 713145-59-6P 713145-61-0P
 - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
- (preparation of [1,7]naphthyridines as PDE4 inhibitors)
- RN 713145-51-8 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

- RN 713145-52-9 CAPLUS
- CN 1-Piperazinecarboxylic acid, 4-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

- RN 713145-55-2 CAPLUS
- CN Acetic acid, 2-[[1-[8-(3-cyanopheny1)-1,7-naphthyridin-6-y1]-4piperidiny1]oxy]-, 1,1-dimethylethyl ester (CA INDEX NAME)

- RN 713145-57-4 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-(3-cyanophenyl)-1,7-naphthyridin-6-yl]-4methyl-, ethyl ester (CA INDEX NAME)

- RN 713145-58-5 CAPLUS
- CN 4-Piperidinecarboxylic acid, 1-[8-[3-(methylthio)phenyl]-1,7-naphthyridin-6-yl]-, ethyl ester (CA INDEX NAME)

- RN 713145-59-6 CAPLUS CN Methanesulfonic aci
 - Methanesulfonic acid, 1,1,1-trifluoro-, 1-[8-[3-(methylthio)phenyl]-1,7-naphthyridin-6-yl]-4-piperidinyl ester (CA INDEX NAME)

- RN 713145-60-9 CAPLUS
- CN 4-Piperidinamine, 1-[8-[3-(methylthio)phenyl]-1,7-naphthyridin-6-yl]- (CA INDEX NAME)

-
- RN 713145-61-0 CAPLUS
- CN 4-Piperidineacetic acid, 1-[8-(3-cyanopheny1)-1,7-naphthyridin-6-y1]-, ethyl ester (CA INDEX NAME)

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